

Application No. 10/827,054
Response dated July 20, 2007

Attorney Docket No. 62041(51588)

Remarks

Claims 1-129 and 142-151 are pending in this application.

Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112.

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, are respectfully requested, as the application is believed to be in condition for allowance.

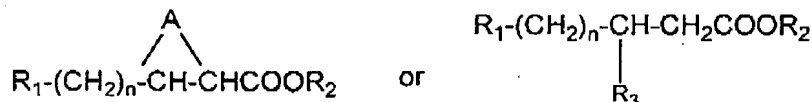
Withdrawal of Earlier Objections/Rejections

Applicants take this opportunity to thank the Examiner for the withdrawal of the prior rejections to the claims under 35 USC §102(b), 103(a), and 112, second paragraph. Applicants further thank the Examiner for the withdrawal of the objection to the information disclosure statement and the acknowledgement of the resubmitted references

Rejections under 35 U.S.C. § 103

Claims 1-4, 7, 9, 11-13, 17, 44-47, 50, 52, 119, 123, 125 and 147-151 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over International Patent Publication No. WO 97/19705 to Elmaleh ("Elmaleh"), in view of United States Patent No. 4,323,547 to Knust, *et al.* ("Knust") and No. 4,524,059 to Elmaleh ("US-Elmaleh").

Elmaleh teaches a fatty acid imaging agent containing a radionuclide in spatial proximity to the stereocenter along the carbon chain of the formulas



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Knust teaches fatty acids labeled with radioactive isotopes, in particular [^{18}F]-fluoroheptadecanoic acid, and their use in methods of investigating the kinetics of myocardial metabolism.

US-Elmaleh teaches a radioactively labeled analog of a fatty acid having an organic substituent bound at the C3, C5, C7 or C9 positions counting from the carboxyl carbon atom, said analog capable of being taken up by mammalian tissue and exhibiting an in vivo beta-oxidation rate below that of the corresponding radioactively labeled fatty acid.

The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Knust by using a [^{18}F]-fluoroheptadecanoic acid as the carbon backbone in Elmaleh. Applicants respectfully disagree and traverse this rejection.

As previously discussed, to properly determine a prima facie case of obviousness, the Examiner "must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made." M.P.E.P. § 2142. This is important as "impermissible hindsight must be avoided and the legal conclusion must be gleaned from the prior art." *Id.* Four factual inquiries must be made: first, a determination of the scope and contents of the prior art; second, a determination of the differences between the prior art and the claims in issue; third, a determination of level of ordinary skill in the pertinent art; and fourth, an evaluation of evidence of secondary consideration. *Graham v. John Deere*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966).

Three criteria may be helpful in determining whether claimed subject matter is obvious under 103(a): first, if there is some suggestion or motivation to modify or combine the cited references; second, if there is a reasonable expectation of success; and third, if the prior art references teach or suggest all the claim limitations. *KSR Int'l Co. v. Teleflex, Inc.* No 04-1350 (U.S. Apr. 30, 2007). With regard to the first criterion, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.3d 690 (Fed. Cir. 1990). "Knowledge in the prior art of every element of a patent claim . . . is not of

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itself sufficient to render claim obvious." *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Teleflex, [Inc. v. Ficosa N. Am. Corp.]*, 299 F.3d 1313, 1333-34 (Fed. Cir. 2002)]. The issue is whether there is an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *KSR Int'l Co. v. Teleflex, Inc.*

As previously argued, the genus of compounds disclosed by Elmaleh is limited to those wherein the $-\text{COOR}_2$ group is bound directly to the cyclic moiety. Nothing in Elmaleh teaches or suggest modifying the compounds to increase the number of carbon atoms between the $-\text{COOR}_2$ group and the cyclic moiety. While Elmaleh discloses a subset of compounds having a C3 bound substituent, this substituent does not form part of a cyclic structure with the remaining fatty acid chain.

Although Knust teaches the use of mid-chain, ^{18}F labeled fatty acids with chain lengths of at least 15 carbon atoms, Knust does not teach or suggest the inclusion of a cyclic moiety at least one carbon atom away from the carboxylic acid thereby allowing a beta-oxidation reaction to occur, thus trapping the labeled analog in bodily tissue.

The Examiner argues that US-Elmaleh "teaches that in order for the first beta-oxidation step to occur the substituent has to be located at the C3 carbon atom." Although Applicants agree with this teaching, applicants further highlight that US-Elmaleh teaches that "the substituent of the analog should be small enough to permit the formation of the first chemical intermediate involved in the fatty acid beta or omega oxidation process; too large a substituent can alter the uptake and behavior of the analog to an undesirably great extent." (Column 2, lines 41-56). Indeed, US-Elmaleh goes on to state that preferred substituents are alkyl or heteroalkyl groups, aryl or heteroaryl groups, and aralkyl and heteroaryalkyl groups. US-Elmaleh does not teach or suggest the use of cyclic moieties within the fatty acid chain itself

One of ordinary skill in the art will readily recognize that the incorporation of a cyclic structure into the backbone of a fatty acid chain will greatly vary the flexibility and spatial conformation of the fatty acid chain as compared to an equal length chain not containing a cyclic structure. Furthermore, the inclusion of a cyclic group will

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produce stereoisomer as well as geometrical isomer unlike those of a corresponding non-cyclic substituted backbone. As such, one of ordinary skill in the art will appreciate that the chemical and steric considerations will likely alter the mechanism for beta-oxidations and thus the reactivity of a given fatty acid in the context of beta-oxidations.

Indeed, the teachings of US-Elmaleh (column 2, lines 41-56) constitute a clear teaching away from the invention as claimed. Thus, one of skill in the art would have lacked motivation to modify the compounds of Elmaleh in light of the beta-oxidation teachings of US-Elmaleh as the C2,C3 cyclic compounds described by Elmaleh would not be expected to be susceptible to beta oxidations of any kind.

Furthermore, given the steric differences, one of skill in the art, in light of the potential to alter the uptake and behavior of the analog to an undesirably great extent would have lacked the motivation to modify the compounds of US-Elmaleh to include fully incorporated cyclic backbone moieties as the organic substituent

Similarly, in light of the uptake considerations described by US-Elmaleh, one of ordinary skill in the art would have lacked the motivation to combine US-Elmaleh with the teachings of Elmaleh and Knust. Nevertheless, even if one were to modify the compounds of Elmaleh with the chain lengths and labeling positions of Knust, one of ordinary skill in the art would have had no expectation of success given the significant potential for altering the ability of the analog to be taken up by the appropriate tissue and become trapped therein.

In sum, one of ordinary skill in the art, without resorting to hindsight, would have had no motivation to combine the Elmaleh, Knust and US-Elmaleh references in light of the potentially contradictory teaching of US-Elmaleh; and without said motivation to combine, one of skill in the art would have had no expectation of success even if one were to try the combination. As such, one of skill in the art would have lacked an apparent reason to incorporate a cyclic moiety into the backbone of a fatty acid chain and to provide for beta-oxidations and without potentially altering the ability of the analog to be taken up by appropriate bodily tissue and become trapped therein to a significant extent.

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Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. § 103 of claims 1-4, 7, 9, 11-13, 17, 44-47, 50, 52, 119, 123, 125 and 147-151.

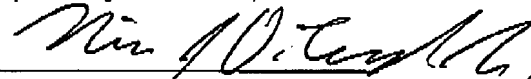
Conclusion

Applicants respectfully request entry of the foregoing remarks into the record of the application, favorable reconsideration and withdrawal of all pending rejections and allowance of the application with all pending claims. If a telephone conference with Applicants' representative would be helpful in expediting prosecution of the application, the Examiner is invited to call the undersigned at the telephone number indicated below.

Applicants do not believe that any fees are required for consideration and entry of this Amendment and Response. Nevertheless, the Director is authorized to charge any required fee or credit any overpayment to Deposit Account No. 04-1105 under order number 62041(51588).

Dated: July 20, 2007

Respectfully submitted,

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